Multi-compartment modelling of diffusion MRI signal shows TE-based volume fraction bias

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Introduction

Diffusion MRI (dMRI) has been widely used to estimate brain tissue microstructure in-vivo. Two of the most widely used microstructural indices are the white matter (WM) and intra-cellular (IC) volume fractions (VF) [2012z,2019f]. In estimating these fractions, a common assumption of dMRI-based signal modeling is to assume that the T2-relaxation for each compartment is equal. However, it has been shown that this assumption is inaccurate [2018v]. Here, we characterize the bias introduced by this assumption using a general multi-compartmental model of the dMRI signal in three distinct scenarios:
3-S0) the realistic-case, where each compartment has its T2-dependent signal at b-value 0 (S0).
2-S0) in which we consider only two separated S0, one for WM and one for CSF similarly to [2014j].
1-S0) a single average S0 is considered for all the compartments, as commonly done in dMRI.
Our simulations and experiments on real data show fitting the WM and IC VF using the more simplistic 2-S0 and 1-S0 model, a systematic bias appears that potentially alters the interpretation of conclusions drawn from studies focusing on WM and IC VF.

Methods

The mathematical formulation of the 3-S0 model defines the signal as the linear combination of the IC, EC and CSF compartments, where the anisotropic components IC and EC are convolved with a Watson distribution, and relies on the definition of the S0 response of each compartment S_0^{ic}, S_0^{ec} and S_0^{csf}. The model depends on several parameters that were determined from the literature or empirically [2018v, 2019f] and are specified in Fig. 1. Assuming that $S_0^{ic}=S_0^{ec}=S_0^{wm}$ we obtain the 2-S0 model and by assuming $S_0^{wm}=S_0^{csf}=S_0$ we obtain the 1-S0 model.

We simulated the signal in 1000 voxels from the 3-S0 model (Fig. 1) with the Human Connectome Project (HCP) acquisition scheme [2013g]. Rician noise was added to obtain a signal noise ratio (SNR) equal to inf, 30, 20 and 10. We fitted WM VF and IC VF using all the three models.
We also considered one subject of the HCP dataset [2013g]. Since the S0 responses of the IC and EC compartments are unknown, in this case we took into account only the 2-S0 and 1-S0 models by computing S_0^{wm} and S_0^{csf} with the Dhollander algorithm [2016d] implemented in Dmipy [2019f].

Results

Fig. 1 shows the distribution of the WM VF and IC VF computed with the 3-S0, 2-S0 and 1-S0 models compared to the ground truth (GT) distribution for each employed SNR. The WM VF is correctly recovered from 3-S0 and 2-S0 models, while it decreases significantly in the case of 1-S0 model. The IC VF is correctly recovered from 3-S0 model, while it increases for 2-S0 and 1-S0 models.The results obtained with distinct SNRs show that the estimation of WM VF is more robust to noise than that of IC VF. Fig. 2 shows the WM VF computed with the 1-S0 and the 2-S0 model on a single slice of the HCP subject. The WM VF recovered via the 2-S0 model is higher than the one found by the 1-S0 model, in accordance to our simulations.

Conclusions

The study of realistic simulated data highlighted how taking into account different T2 responses for each modelled compartment allows to achieve an unbiased estimation of WM VF and IC VF. When multi-echo data are not available, the 2-S0 formulation still improves the approximation of the WM VF, while the IC VF is systematically overestimated. Given the bias introduced by the employment of the 1-S0 model and the natural applicability of the 2-S0 model using only dMRI data [2016d], we recommend the use of multi-S0 models to study WM VF and IC VF.

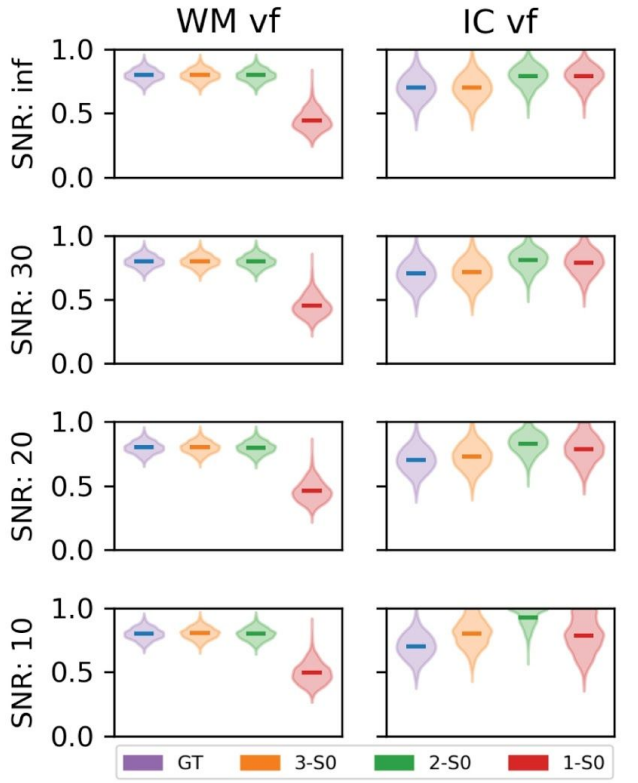
Figure 1

The signal S is defined as the linear combination of the IC, EC and CSF compartments, where the anisotropic components IC and EC are convolved with a Watson distribution W of parameters d and k. The signal shape each compartment Ex depends on the characterising diffusivities and the S0 responses are designed for defining the 3-S0 model. Each parameter in the table was drawn from a normal distribution of mean and standard deviation equal to the ones listed. The S_0^{ic} and S_0^{ec} values were computed as S_0^{x}=6000 $e^{0.089}/TE_x$ [2018v]. The value for the S0 response of the white matter compartment was defined as $S_0^{wm}=f_{ic}S_0^{ic} + f_{ec}S_0^{ec}$ and the parameters for S_0^{csf} were determined empirically [2016d]. The radial diffusivity

was set to dr= 3x10-3 and the direction of the anisotropic compartment was drawn as a random 3D vector of unitary length. Each plot shows the distribution of the estimated white matter and intra cellular volume fractions computed from the 3-S0, 2-S0 and 1-S0 formulations against the ground truth (GT) for each considered SNR.

$$S = f_{wm} \cdot W(d,k) * \left[f_{ic} \cdot S_0^{ic} \cdot E^{ic}(\lambda_\parallel) + (1 - f_{ic}) \cdot S_0^{ec} \cdot E^{ec}(\lambda_\parallel, \lambda_\perp) \right] + (1 - f_{wm}) \cdot S_0^{csf} \cdot E^{csf}(\lambda_r)$$

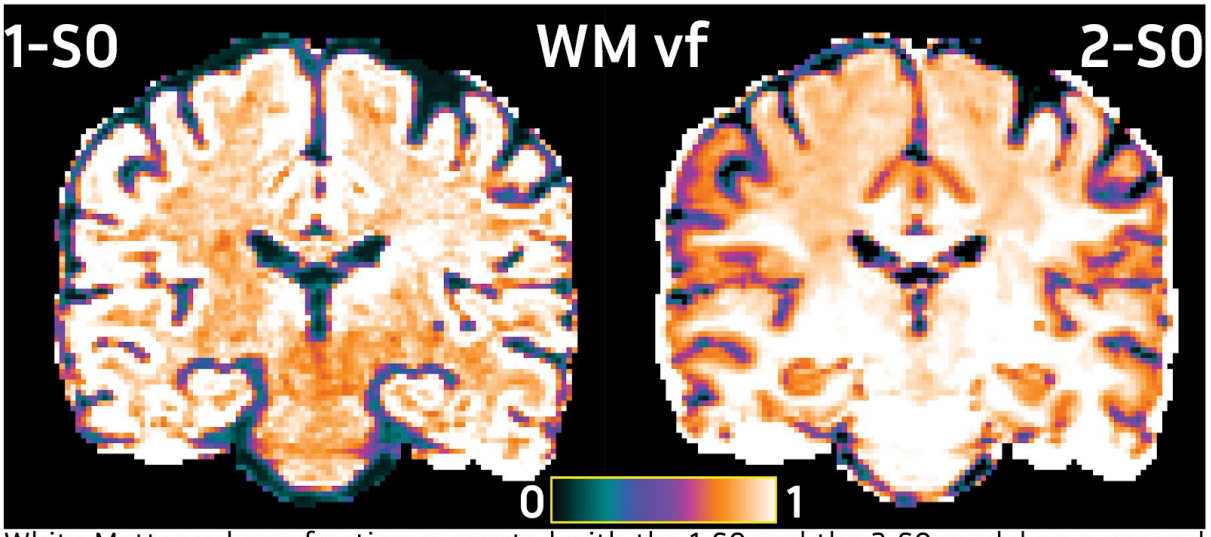
	μ	σ		μ	σ
f_{ic}	0.7	0.1	f_{wm}	0.8	0.05
$d_\parallel$	$2 \cdot 10^{-3}$	10^{-4}	$d_\perp$	$5 \cdot 10^{-4}$	$5 \cdot 10^{-5}$
k	16	4	TE_{ic}	$9 \cdot 10^{-2}$	10^{-2}
TE_{ec}	$6 \cdot 10^{-2}$	$5 \cdot 10^{-3}$	$S0_{csf}$	10^4	$5 \cdot 10^2$



The **signal S** is defined as the linear combination of the IC, EC and CSF compartments, where the anisotropic components IC and EC are convolved with a Watson distribution W of parameters d and k. The signal shape each compartment E^s depends on the characterising diffusivities and the S0 responses are designed for defining the 3-S0 model. Each parameter in the **table** was drawn from a normal distribution of mean and standard deviation equal to the ones listed. The $S0ic$ and $S0ec$ values were computed as $S0x{=}6000\ e^{0.089/TEx}$ [2018v]. The value for the S0 response of the white matter compartment was defined as $S0wm{=}f_{ic}S0_{ic} + f_{ec}S0_{ec}$ and the parameters for $S0csf$ were determined empirically [2016d]. The radial diffusivity was set to $d_r = 3x10^{-3}$ and the direction of the anisotropic compartment was drawn as a random 3D vector of unitary length. Each **plot** shows the **distribution** of the estimated white matter and intra cellular volume fractions computed from the 3-S0, 2-S0 and 1-S0 formulations against the ground truth (GT) for each considered SNR.

Figure 2

White Matter volume fraction computed with the 1-S0 and the 2-S0 model on a coronal slice of HCP subject 473952. The 2-S0 model shows higher WM volume fraction in WM regions with respect to the 1-S0 model. The S0 responses for the WM and CSF compartment where computed using the Dhollander algorithm [2016d] implemented in Dmipy [2019f].



White Matter volume fraction computed with the 1-S0 and the 2-S0 model on a coronal slice of HCP subject 473952. The 2-S0 model shows higher WM volume fraction in WM regions with respect to the 1-S0 model. The S0 responses for the WM and CSF compartment where computed using the Dhollander algorithm [2016d] implemented in Dmipy [2019f].

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Acknowledgements

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